

**ABSTRACT OF THE DISCLOSURE**

The invention is directed to oligonucleotides and oligonucleosides functionalized to include lipophilic moieties and having improved biostability and altered biodistribution in mammals. In one embodiment, such lipophilic oligonucleotide conjugates are used in a method of targeting antisense oligonucleotides to hepatic tissues and thereby preferentially modulating gene expression in the liver and associated tissues of a mammal.